

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
2-HYDROXYPROPYLMETHANETHIOSULFONATE

Chemical Code # 000972, Tolerance # 50119
SB 950 # 708
5/20/03

I. DATA GAP STATUS

Chronic toxicity, rat:	Data gap, no study submitted
Subchronic dermal, rat	Data gap, inadequate study, no adverse effect indicated
Chronic toxicity, dog:	Data gap, no study submitted
Oncogenicity, rat:	Data gap, no study submitted
Oncogenicity, mouse:	Data gap, no study submitted
Reproduction, rat:	Data gap, no study submitted.
Teratology, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rabbit:	Data gap, inadequate study, no adverse effect indicated
Gene mutation:	Data gap, inadequate study, no adverse effect indicated
Chromosome effects:	No data gap, no adverse effect
DNA damage:	Data gap, inadequate study, no adverse effect indicated
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.

All record numbers through 131024 were examined.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T030520

Original: Kishiyama and Gee, 5/20/03

2-Hydroxypropylmethanethiosulfonate (HPMTS) is an antimicrobial pesticide registered in California for food processing water systems. In December of 1995, the US Environmental Protection Agency issued a "Reregistration Eligibility Decision" for this chemical. They consider it to be corrosive and severely irritating to the skin and eyes. Based on the non-food use pattern, the Agency was not requiring chronic, oncogenicity or reproductive studies as of 1995, as there is not likely to be significant human exposure. With the exception of the dose range-finding study for the subchronic rat dermal study, all of those pertinent to human health effects under SB950 for

Tier 1 as an antimicrobial are on file with the Department of Pesticide Regulation.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

CHRONIC TOXICITY, RAT

Subchronic:

006 131024 Siglin, J. C. "91-Day Dermal Study in Rats with HPMTS." (Springborn Life Sciences, Inc., SLS Study No. 3138.9, December 15, 1988.) HPMTS (purity not stated, lot # SLH) was administered dermally (6 hours/day, 5 days/week for 13 weeks) at doses of 0, 10, 50, or 250 mg/kg/day to 10 Sprague-Dawley rats/sex/group. Skin irritation was dose related in incidence and severity. Dermal NOEL <10 mg/kg/day. Hematological changes (reduced erythrocytes, hemoglobin and hematocrit) were noted for the high dose groups. Systemic NOEL = 50 mg/kg/day (lower body weight in males at 250 mg/kg/day). Serum chemistry changes (lower glucose and higher creatinine) were reported as not biologically significant. UNACCEPTABLE. Upgradeable (test article purity and test solution preparation). (Kishiyama and Gee, 5/19/03).
EPA: LOEL = 250 mg/kg/day and NOEL = 50 mg/kg/day based on body weight and hematology.

CHRONIC TOXICITY, DOG

No Study Submitted.

ONCOGENICITY, RAT

No Study Submitted.

ONCOGENICITY, MOUSE

No Study Submitted.

REPRODUCTION, RAT

No Study Submitted.

TERATOLOGY, RAT

004 114156 Rodwell, D. E. "Teratology Study in Rats with HPMTS." (Springborn Life Sciences, Inc., SLS Study No. 3138.11, December 8, 1988.) HPMTS (lot # SLH, no purity stated) was administered *via* gavage in aqueous solution at doses of 0 (distilled water), 10, 30, or 75 mg/kg/day during gestation days 6 through 15 to 28 Sprague-Dawley COBS®CD® mated female rats. Dosing solutions were not corrected for purity. At 75 mg/kg/day, there were 2 treatment-related deaths, lower bodyweight and food consumption and an increase in clinical signs including rales, labored breathing, dark material around nose and mouth and decreased activity. At 30 mg/kg, clinical signs noted at 1 hour postdosing included nasal discharge and salivation. Maternal NOEL = 10 mg/kg/day. No treatment-related fetal malformations were reported. Although the mean fetal weight for the 30 and 75 mg/kg/day groups were 3.4 g versus 3.5 g for control groups, the difference was not statistically significant. Developmental NOEL \geq 75 mg/kg/day. UNACCEPTABLE. Upgradeable (test article characterization). (Kishiyama and Gee, 5/16/03).
EPA: Maternal NOEL = 10 mg/kg/day and developmental NOEL = 10 mg/kg/day (reduced fetal weight)

007 074325 Duplicate of 114156.

007 074569 Rodwell, D. E. "Pilot teratology study in rats with HPMTS." (Springborn Life Sciences, SLS Study No. 3138.10, June 15, 1988) HPMTS (lot # SLH, no purity stated) was given by gavage to groups of 8 Sprague-Dawley COBS®CD® rats at doses of 0 (water), 10, 25, 50, 75, 100, 150 or 300 mg/kg/day, days 6 through 15 of gestation. Dose solutions were not adjusted for purity. Body weights were recorded on days 0, 6, 9, 12, 16 and 20. On day 20, the females were sacrificed and the uterine contents examined for viable fetuses and early and late resorptions. Viable fetuses were weighed and discarded. Survival was 100 % at 10, 25 and 50 mg/kg/day. There were 1, 1, 5 and 5 deaths between day 6 and day 17 at doses of 75, 100, 150 and 300 mg/kg/day, respectively. Clinical signs increased in incidence and frequency with increasing dose, especially at 150 and 300 mg/kg/day. Signs included gasping, labored breathing, salivation, decreased activity and dark material around the mouth. Maternal body weights were comparable up to 100 mg/kg/day but were reduced at 150 and even more so at 300 mg/kg/day. Fetal weights were unaffected up to 100 mg/kg/day but were reduced slightly at 150 and 300 mg/kg/day. No external fetal abnormalities were noted. Supplemental study. No worksheet. (Gee, 5/20/03)

TERATOLOGY, RABBIT

005 114157 Rodwell, D. E. "Teratology Study in Rabbits with HPMTS." (Springborn Life Sciences, Inc., SLS Study No. 3138.13, December 8, 1988.) HPMTS (lot # SLH, purity not stated) was administered *via* gavage in aqueous solution at doses of 0 (distilled water), 0, 0.75, 4.0 or 7.5 mg/kg/day during gestation days 6 through 18 to 20 artificially inseminated New Zealand White rabbits. Reduced bodyweight gain and food consumption was marginal for high dose does. Maternal NOEL = 4.0 mg/kg/day. There were treatment-related clinical signs or fetal malformations/variations. Developmental NOEL = >7.50 mg/kg/day. UNACCEPTABLE. Upgradeable (test article characterization). (Kishiyama and Gee, 5/16/03).
EPA: Maternal NOEL = 0.75 mg/kg/day (decreased body weight) and developmental NOEL > 7.5 mg/kg/day.

008 074326 Duplicate of 005 114157.

008 074570 Rodwell, D. E. "Pilot teratology study in rabbits with HPMTS." (Springborn Life Sciences, Study No. 3138.12, August 25, 1988). HPMTS (lot # SLH, purity not stated) was given to groups of 6 presumed pregnant New Zealand White rabbits by oral gavage at doses of 0 (water), 10, 30, 60, 100 or 150 mg/kg/day, gestation days 6 through 18. Dose solutions were not corrected for purity. Body weights were recorded on days 0, 6, 9, 12, 18, 24 and 29. Cesarean sections were performed on day 29, fetuses examined externally, weighed and discarded. There were 1, 3, 3, 5 and 5 deaths between days 7 and 17 at 10, 30, 60, 100 and 150 mg/kg/day, respectively. Treatment-induced clinical signs included gasping, labored breathing or rales, decreased activity, partial loss of limb activity, tremors, urine staining and ocular or nasal discharge. One rabbit each aborted at 10, 30 and 60 mg/kg/day. There were 6, 4, 2, 2, 1 and 1 animals at terminal sacrifice with increasing dose. The single animal at 150 mg/kg had total litter resorption. There were no external fetal abnormalities. Mean fetal weight was reduced at 60 and 100 mg/kg/day. The author concluded that 10 mg/kg/day was too high for the definitive study. Supplemental data. No worksheet. (Gee, 5/20/03)

GENE MUTATION

003 062456 Jagannath, D. R. "Mutagenicity Test on HPMTS in the Ames *Salmonella*/Microsome Reverse Mutation Assay." (Hazleton Laboratories America, Laboratory Project ID HLA Study No. 9786-0-401, May 1, 1987) HPMTS (purity not stated, lot 7-0260, clear yellow liquid) was assayed for mutagenicity at concentrations ranging from 0.01 to 0.50 µl/plate with and without rat liver metabolic activation (S9 Mix) using *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538. There were two trials with triplicate plates per concentration per trial. There was no significant increase in revertants with HPMTS treatments. UNACCEPTABLE. Upgradeable (test article purity). (Kishiyama and Gee, 5/15/03).

CHROMOSOME EFFECTS

** 003 062455 Murli, H. "Mutagenicity Test on HPMTS in an *In Vitro* Cytogenetic Assay Measuring Sister Chromatid Exchange Frequencies in Chinese Hamster Ovary (CHO) Cells." (Hazleton Laboratories America, Inc., HLA Study No.: 9973-0-438, August 10, 1987.) HPMTS (lot J.M.V., 80% from record 062454, 1.29 g/ml) was evaluated for genotoxicity at concentrations ranging from 0 (medium) and 0.167 to 5020 µg/ml, with and without rat liver metabolic activation (S9 Mix) using Chinese Hamster ovary (CHO-WBL) cells. Test article was converted to weight/volume to prepare the test solutions. There was a single culture per concentration, rather than the recommended 2. Cultures were exposed for approximately 25 hours without activation and for 2 hours with activation followed by an additional incubation period. BrdUrd was included in the incubation medium to visualize the SCEs. Fifty cells per culture were scored for sister chromatid exchanges in M2 and 100 cells were surveyed to determine mitotic delay. No cell cycle delay was noted in the cultures scored, therefore only one harvest time was used. Test results indicated no induction of reciprocal chromatid exchanges in CHO cells. ACCEPTABLE with deficiencies. Although there was only a single culture per concentration, there was no indication of an adverse effect to concentrations with significant toxicity (50.2 µg/ml). (Kishiyama and Gee, 5/13/03).

DNA DAMAGE

50119 - 003 062454 Cifone, M. A. " Mutagenicity test on HPMTS in the rat primary hepatocyte unscheduled DNA synthesis assay." (Hazleton Laboratories America, Inc., HLA 9973-0-447, November 3, 1987) HPMTS (lot J.M.V., 80% by weight, density of 1.29 g/ml) was tested with primary rat hepatocytes from a male Fischer 344 rat. Concentrations tested ranged from 0.5 to 5000 ug/ml, 18-hour exposure, in triplicate for UDS with two additional cultures for cytotoxicity by trypan blue dye exclusion. Cultures at 1.0 to 50.0 ug/ml were suitable for analysis, with a total of 150 nuclei scored per concentration. There was no increase in net nuclei grain counts with treatment. 2-Acetylaminofluorene, the positive control, was functional. Evaluated as UNACCEPTABLE but upgradeable with submission of the cytoplasmic and nuclear grain counts for each coverslip and information regarding whether the 80% purity was considered in the preparation of the test solutions. (Kishiyama and Gee, 5/12/03)

NEUROTOXICITY

Not required at this time.